Proposed synopsis on

PHYTOCHEMICAL AND PHARMACOLOGICAL EVALUATION OF NEUROPROTECTIVE POLY HERBAL REMEDY TARGETED FOR ALZHEIMER'S DISEASE

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INTRODUCTION:

Every single portion of the plant is referred to as "herb." As far back as 4,000 years ago, people began using plants as medicine. Medicinal plant treatments are regarded as safe because of their low risk of adverse consequences. Up to 80% of plant-based medications come from China and India. Nowadays, the development of pharmaceuticals depends heavily on medicinal herbs. For the majority of their medical needs, about 75% of people worldwide rely on plants or plant extracts. In spite of the remarkable progress in knowledge of the CNS functions and structure, discovery of novel drugs along with their development for several central nervous system disorders have been challenging [1].

Alzheimer's disease (AD) is a neurodegenerative disease affecting older adults.AD is characterized by memory loss, behaviour, deterioration, performance impairment, and thought slowness. The condition is reproduced by severe depression [2].As per WHO, in 2023, more than 55 million people worldwide have dementia, with 60–70% of those cases estimated to be Alzheimer's diseaseover 60% of whom live in low and middle-income countries. Nearly 10 million new cases of dementia develop each year. The number of people with dementia is expected to triple by 2050[3]. Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by personality and behavioural impairment along with dementia. AD is a condition of high neurofibrillary tangles(NFTs) in specific brain region and β-amyloid level due to duplication or mutation of β-amyloid precursor proteins (APP) and a presenilin-encoding gene for proteolytic enzymes [4].

In the past few years there has been increasing attention to the epigenetic mechanisms involved in AD. Epigenetic modifications are defined as heritable but reversible changes in chromatin structure associated with alterations in gene expression. The significant role of epigenetic mechanisms for brain activities and neuropathology has become increasingly clear. Research investigating the dynamic epigenetic regulation of AD is a field still in its infancy and new insights into the epigenetic regulatory mechanisms of AD are necessary to improve our understanding of the disease[5].

Alzheimer's is the most common form of dementia. Other types of dementia

- Alzheimer's disease accounts for 50 to 70% of the cases of dementia.
- Vascular dementia.

- Mixed dementia is a condition in which Alzheimer's disease and vascular dementia occur together.
- Parkinson's disease affects the control of movement, resulting in tremors, stiffness, and impaired speech.
- Dementia with Lewy bodies often starts with wide variations in attention and alertness.
- Huntington's disease is an inherited, progressive disorder that causes irregular movements of the arms, legs, and facial muscles [6].

Several of today's modern manufactured pharmaceuticals have their origins in the plant world and herbal remedies led to the main pharmacopeia only around two hundred years ago. Herbal medicine is currently in the front line as an alternative measure to Alzheimer's neurological disorder. Some herbs have the ability to improve brain function [7].

According to researchers AD symptoms usually appear after age 60, but in some cases, the early form of the disease is associated with some kind of genetic defect.The etiology is unknown, but it is clear that genetic factors play a role in 10% of cases, up to 15% of cases.

Medicines for AD available Donepezil(Aricept), Rivastigmine (Exelon), Galantamine (Razadyne), formerly called Reminyl) and Memantine (Namenda).

Other medicines may be needed to control aggressive, agitated or dangerous behaviours such as haloperidol, Risperidone and Quetiapine. These are usually given in very low doses due to the risk of side effects including an increased risk of death [8].

The treatment of Alzheimer's disease remains a challenging task in modern medicine, as the development of Alzheimer's disease is a complex process involving both genetic and environmental factors. Therefore, medicinal plants are considered to be a novel and promising source of potential anti-Alzheimer's drugs.

Medicinal plants are considered promising for the treatment of Alzheimer's disease due to their cognitive effects as well as their mechanism ofaction on the basic pathophysiology of the disease.

Our study identified several medicinal plants with potential therapeutic effects against Alzheimer's disease. However, no serious adverse events were reported [8].

A range of traditional plants imparts effects via acetylcholinesterase activity, β-amyloid peptide formation in plaques, neurotrophic factors and through antioxidant activity. It is necessary to look for more effective treatment for AD with the minimum side effects. According to WHO,

presently 80 % of the world's population relies on traditional medicines and plant extracts and the active constituents are used to meet people's primary health care needs. Plants contain rich source of primary and secondary metabolites for improving health problems.

Pharmaceutical industry is facing some challenges like elevated cost and unendurable risk management due to the high burden of neurodegenerative disorders. A significant shift of drug discovery is being witnessed from synthetic moieties to herbal formulation.

So, attempt has to develop polyherbal formulation/nutraceutical targeting epigenetic changes for eradicationof AD generation to generation.

Need of study:

Alzheimer's disease is one of the leading neurodegenerative disease that affects a large number of elderly (late-stage AD) as well as adults (familial AD).

It gradually impairs memory and reasoning and, eventually, the capacity to do even the most basic tasks. It constitutes for the pathogenesis of majority of AD cases that affects around 55million people globally.

Every year, there are nearly 10 million new cases reported.

There are very few treatment options available for AD therapy and these targets AD primarily at amyloid and tau pathology, that are still in the drug pipeline and not yet available in market.

Secondarily, by either inhibiting acetylcholinesterase (such as galantamine, donepezil, rivastigmine and tacrine) or preventing the damage to cholinergic neurons by glutamate (such as memantine).

It is necessary to look for more effective treatment for AD with the minimum side effects both primarily as well as secondarily.

REVIEW OF LITERATURE:

1. **Parul Agarwal et al (2013)**

According to researchers AD symptoms usually appear after age 60, but in some cases, the early form of the disease is associated with some kind of genetic defect.

The cause is unknown, but it is clear that genetic factors play a role in 10% of cases, up to 15% of cases. AD of two types one is Early onset AD (before age 60) and second is Late onset AD (after age 60). Medicinal plants are considered promising for the treatment of Alzheimer's

disease due to their cognitive effectsandmore importantly their mechanism of action on the basic pathophysiology of the disease [8].

2. **Nusrat Zahan Bhuiyan et al (2023)**

In this study the researcher focus on genetic factors behind Alzheimer's disease and their association with foods and their relationships with cognitive dysfunction.

It takes look at dietary patterns and economic challenges in Alzheimer's disease prevention [9].

3. **P.Mecocci et al (2014)**

Numerous chemical compounds from classes of natural dietary sources exhibit protective effecs against certain age-related illnesses, including neurodegenerative diseases especially Alzheimer's disease (AD). These substances, referred to as nutraceuticals. Structurally, they function at various biochemical and metabolic levels and have demonstrated various kinds of neuroprotective characteristics [10].

4. **Jogender Mehla et al (2020)**

This review focused on Alzheimer's disease (AD) is the primary cause of cognitive impairment. Progressive memory loss, linguistic impairments, anxiety, despair, mood swings, and psychosis are some of its hallmarks. While the characteristics of AD are

In addition to cholinergic failure, β-amyloid plaques, and the production of neurofibrillary tangles, it is linked to additional neurotransmitter dysfunction, increased levels of advanced glycation end products, oxidative damage, neuroinflammation, and environmental and hereditary variables. In the present article, the experimental and clinical evidence have been reviewed for various Indian herbal medicines such as *Centella asiatica, Bacopa monnieri, Curcuma longa, Clitoriaternatea, Withaniasomnifera, Celastrus paniculatus, Evolvulus alsinoides, Desmodiumgangeticum, Eclipta alba, Moringa oleifera* and*Convolvuluspluricaulis,* which have shown potential in cognitive impairment. Some commonly available herbal formulations for memory impairment in India have also been reviewed [12].

5. **NafaaAlzobaidi et al (2021)**

In this work discuss regarding role of common medicinal plants, which are widely used in various traditional systems of medicine as potential preventative or treatment strategies against AD. Herbal plants and photoactive compounds are superior in terms of safety when compared with synthetic drugs such as donepezil, and considered as promising alternative strategies for

improving memory deficits. In traditional Indian and Chinese systems of medicine, green tea is also used for the treatment of obesity, diabetes mellitusand neuroinflammation [13].

6. **Sushma Pradeep et al (2020)**

In this wok discuss regarding combination drugs are gaining importance and progress in pharmaceutical technology as they act on multi-mode targets responsible for the cause of AD. These products increase clinical effectiveness, reduce administrative costs, and enhance the patients' adherence capacity. Combinational therapies are not found to be associated with adverse effects as they can overcome toxicity by accessing multi-target mechanisms [14].

7. **Rammohan V Rao et al (2012)**

According to researcher drugs made from medicinal plants are becoming more and more popular, and their scientific and commercial significance seems to be growing in areas related to the environment and health [15].

8. **Wu et al. Clinical Epigenetics (2023)**

Epigenetic memory is essential for life that governs the predefined functional features of cells. Recent evidence has indicated that the epigenetic modification provides a potential link to gene expression changes that may be involved in the development of various chronic diseases, and targeting the epigenome becomes a plausible method for treating diseases. Traditional herbal medicine has gradually entered the vision of researchers due to its low toxicity and its effectiveness in treating diseases. This review summarized the impact of herbal medicine and its bioactive components on disease epigenome as examples of how utilization of epigenetic plasticity could be useful as the basis for the future development of targeted therapies in chronic diseases [16].

9. **Toufik Abdul-Rahman et al. (2023)**

In this work discuss regarding Curcumin which is integral component of traditional medicine in numerous cultures world-widehas collect interest as a promising AD treatment. Current research indicates that curcumin may exhibit therapeutic potential in neurodegenerative pathologies, attributed to its potent anti-inflammatory and antioxidant properties. Additionally, curcumin and its derivatives have demonstrated an ability to modulate cellular pathways via epigenetic mechanisms [17].

10. Yi-Ping Zhu et al. (2015)

There are many different epigenetic modification mechanisms which interact with and influence each other and finally participate in the pathogenesis of AD. Therefore, different epigenetic mechanisms might target specific disease processes, and the future epigenetic therapy of AD should be comprehensive. Moreover, it is necessary to find a new effective pathway which acts on specific epigenetic mechanisms in specific genes or sets of genes while avoiding side effects on others. The specificity requirements for an AD epigenetic therapeutic agent will be challenging. According to integrative medicine, the interaction of genetic, epigenetic, and environmental toxins might be the real cause of AD, and also the current cocktail treatment of AD indicates that it is important for us to investigate in detail the epigenetic mechanisms in AD [18].

11. Chinaza Godswill Awuchi et.al. (2023)

This work discussed regarding some complementary and alternative medicine in treating disorders of central nervous system Complementary and alternative system of medicine could rely on practices of traditional medicine, e.g. traditional medicine in Africa, Ayurveda in India, traditional Chinese medicine, etc., to treat some diseases such as CNS disorders, infections, etc. Few beneficial uses of traditional medicine have been studied [19].

12. Chiara Villa et al. (2024)

Epigenetic modifications have been implicated in a number of complex diseases as well as being a hallmark of organismal aging. Several reports have indicated an involvement of these changesin Alzheimer's disease (AD) risk and progression, most likely contributing to the dysregulation ofAD-related gene expression measured by DNA methylation studies. Given that DNA methylation istissue-specific and that AD is a brain disorder, the limitation of these studies is the ability to identifyclinically useful biomarkers in a proxy tissue, reflective of the tissue of interest, that would be lessinvasive, more cost-effective, and easily obtainable [20].

13. Oliwia Stefaniaket al.(2022)

Alzheimer's disease is a progressive brain disease that is becoming a major health problem in today's world due to the aging population. Despite it being widely known that diet has a significant impact on the prevention and progression of Alzheimer's disease, the literature data are still scarce and controversial. The application of the principles of rational nutrition for the elderly is suggested for Alzheimer's disease. The diet should be rich in neuroprotective

nutrients, i.e., antioxidants, B vitamins, and polyunsaturated fatty acids. Some studies suggest that diets such as the Mediterranean diet, the DASH (Dietary Approaches to Stop Hypertension) diet, and the MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet have a beneficial effect on the risk of developing Alzheimer's disease [21].

14. **C. Castillo-Rangel et.al.(2023)**

Among the animal models found, the rat model has been the most studied in terms of mood/affective disorders. We believe that more studies are needed where molecular changes are correlated with animal behavior of AD. The mood disorders studied are depression, anxiety, dysthymia, bipolar disorder, and drug-induced affective disorders [22].

15. **Dimitrios Athanasopoulos et al. (2015)**

Epigenetics is becoming a very attractive subject for researchers because it can shed light on unknown aspects of complex diseases like AD.DNA methylation, histone modifications, and microRNAs are the principal epigenetic mechanisms involved in AD pathophysiology. Nutrition is anenvironmental factor that is related to AD through epigenetic pathways. Vitamin B-12, for instance, can alter the one-carbonmetabolism and thus interfere in the DNA methylation process.Nutrition might grow to become a preventive and even therapeutic alternative against AD [23].

Hypothesis:

The treatment of Alzheimer's disease remains a challenging task in modern medicine, as the development of Alzheimer's disease is a complex process involving both genetic and environmental factors.Therefore, medicinal plants are considered to be a novel and promising source of potential for challenging diseases.Medicinal plants are considered promising for the treatment of much neuronal disorders, due to their cognitive effects andmore importantly their mechanism of action on the basic pathophysiology of the disease.

Epigenetic changes encompass modifications to DNA, histones, and microRNAs that can influence gene expression. Aberrant epigenetic changes can perturb key cellular processes, including cell cycle control, intercellular communication, DNA repair, inflammation, stress response, and apoptosis. Such disruptions can contribute to cancer development by altering the expression of genes involved in tumorigenesis. However, these modifications are reversible, offering a unique avenue for therapeutic intervention. Plant secondary compounds, including

terpenes, phenolics, terpenoids, and sulphur-containing compounds are widely found in grains, vegetables, spices, fruits, and medicinal plants.Diets rich in lycopene (found in tomatoes) and low-carbohydrate, ketogenic regimens are being studied for their roles in prevention and treatment.Epigenetic alterations play a crucial role in AD by affecting pathways that control cell growth, differentiation, and apoptosis.

Numerous plant-derived compounds have demonstrated the potential to target abnormal epigenetic modifications, including apigenin (histone acetylation), berberine (DNA methylation), curcumin (histone acetylation and epi-miRs), genistein (histone acetylation and DNA methylation), lycopene (epi-miRs), quercetin (DNAmethylation and epi-miRs)etc.

abnormal epigenetic alterations and discusses the promising efficacy of plant-derived compounds in mitigating these deleterious epigenetic signatures in human neurological disorders.

Although the pathogenesis and symptoms related to AD have been established, the pathways that lead to the development of these symptoms and pathogenesis of AD are poorly known. However, the involvement of genetic factors in the pathogenesis of AD has been established in approximately 70% of cases and involves multiple genes.Besides, there is no cure for AD in current time and the available therapeutics provide only symptomatic relief without affecting the underlying pathogenesis of AD. The gene-based therapeutics and drug targets have shown incredible and appreciable advances in alleviating human sufferings and complexities.

So, it is urgent need to have suitable remedy to prevent AD at genetic level through consideration of molecular changes in disease progression.

Objectives:

- To select and extract or procure pure neuroprotective extract which having preventive epigenetic constituents.
- To prepare poly-herbal remedy targeting preventive Pharmacological potentials for Alzheimer's diseaseand carry out Phytochemical evaluation and its characterization study as per standard guidelines.
- To carry out *In-vitro*/*In-silico* and *In-vivo*activity study for Pharmacological potentials of prepared poly-herbal remedy.

Plan of work:

a) Literature survey.
b) Selection of suitable medicinal plants and Extraction or procurement of pure extract of selected medicinal plants.
c) Prepare poly-herbal remedy, photochemical evaluation and characterization study of prepared remedy.
d) Pharmacological Screening for Alzheimer's disease (As per suitability, availability, advancement and current needs, animal models will be taken for screening) as per followings.
   - Scopolamine Induced Amnesia Model
   - $AlCl_3$ Induced Alzheimer's disease
e) Statistical interpretation

MATERIAL & METHODS:

1. PreliminaryPhytochemical Investigation

Phytochemical examination of selected plants will be carried out as per the standard methods [24-25].

2. Scopolamine Induced Amnesia Model

Induction of Alzheimer's disease: Alzheimer's disease mainly induced by using Scopolamine into the Wistar Rats[11].

- **Behavioural studies:**

a. Elevated plus-maze

Rodent learning and memory will be assessed using the Elevated Plus Maze (EPM), an exteroceptive behavioural paradigm [11].

b. Morris water maze (MWM) task

The MWM task will be used to gauge rat's capacity for spatial long-term memory [11].

c. Y-maze task

Y-maze task will be used to measure the spatial working through the spontaneous alternation of behaviour [11].

d. Measurement of acetylcholine esterase (AChE) content

The content of AChE in the brain tissues of control and treated animals will be accessed by the method of Shunan Diet al [11].

e. Histopathological study

Histopathology of brain cortex and dentate gyrus of rat brain will be performed.

3. $AlCl_3$ Induced Alzheimer's disease Model

Induction of Alzheimer's disease: Alzheimer's disease mainly induced by using Aluminium Chloride into the Wistar Rats [11].

- **Behavioural studies:**

a. Radial arm maze (RAM) test

The RAM test will be performed according to Shunan Diet al.[11].

b. **Morris water maze (MWM) task:**

The MWM task will be used to gauge rat's capacity for spatial long-term memory [11].

c. Measurement of acetylcholine esterase (AChE) content

The content of AChE in the brain tissues of control and treated animals will be accessed by the method of Shunan Di. et al [11].

d. Histopathological study

Histopathology of brain cortex and dentate gyrus of rat brain will be performed.

4. Data and statistical analysis:

Data were illustrated as mean ± SD of triplicate experiments and determined using SPSS version 17.0 statistical software. The comparisons between the experimental groups were executed using ANOVA followed by Student-Newman-Keuls multiple comparison assay. $p < 0.05$ was considered as statistically significant [11].

Duration of Work:

Sr. No.	Activity	Tentative Duration (Months)	Tentative Duration (Years)
1	Literature Survey	06	01
2	Selection and collection of suitable Indian medicinal plants	03	
3	Extraction of selected medicinal plants	03	
4	Phytochemical analysis of plant extracts	03	01
5	Pharmacological Screening for Alzheimer's disease with publication	09	
6	Compilation, interpretation of data and conclusion	06	01
7	Writing of thesis	03	
8	Publishing research and submitting data	03	
9	Total	36	03

Research Outcome:

The most advanced type of neurodegenerative disease that significantly reduces cognitive function is Alzheimer's disease (AD). It has been determined that oxidative stress plays a role in the pathophysiological pathways of several neurodegenerative disorders. It is estimated that 50 million people worldwide have been diagnosed with AD, and by 2050, this number might rise to almost 152 million. AD is currently the sixth most common cause of death for people of all ages and the fifth most common among those 65 and over. The majority of AD cases are recorded in underdeveloped nations. Approximately 68% of senior patients are often from South Asian, Chinese, and Indian nations.Tacrine, dopnezil, aniracetam, piracetam, and rivastigmine are examples of synthetic medications used to treat cognitive dysfunction and memory loss related to AD. However, these medications have serious side effects, such as gastrointestinal issues and issues with their absorption.

The active ingredients in plant extracts and traditional medicines are currently utilized to treat the main health care needs of 80% of the world's population. A wealth of primary and secondary metabolites found in plants can help with a variety of health issues. The increased prevalence of neurodegenerative diseases presents the pharmaceutical business with interesting issues,such as high costs and intolerable risk management.

The current study is being considered to test herbal plants for Alzheimer's disease based on scientific facts.

REFERENCES:

1. Chinaza Godswill Awuchi.Plants, phytochemicals, and natural practices in complementary and alternative system of medicine for treatment of central nervous system disorders. Int. J. Food Prop.2023; 26(1):1190-1213. DOI: 10.1080/10942912.2023.2205039.
2. Muhammad Akram,Allah Nawaz.Effects of medicinal plants on Alzheimer’s disease and memory deficits.Neural Regen. Res.2017,April;12(4):660-670. DOI: 10.4103/1673-5374.205108.
3. World Health Organization.2023, March 15.
4. Muhammad Kamran, Rehana Kousar, Shakir Ullah, Siraj Khan, Muhammad Farooq Umer, Haroon Ur Rashid, Zakir Khan, Muhammad Ijaz Khan Khattak and Mujeeb Ur

Rehman.Taxonomic Distribution of Medicinal Plants for Alzheimer's Disease: A Cue to Novel Drugs.International Journal of Alzheimer's Disease.2020;1-15.
DOI:10.1155/2020/7603015.

5. S.Davinelli,V.Calabrese,D. Zella,G. Scapagnini.Epigenetic Nutraceutical Diets in Alzheimer's Disease.J Nutr Health Aging.2014;18(9):800-805.
6. Anil Kumar Singhal, Vijay Naithani, Om Prakash Bangar. Medicinal plants with a potential to treat Alzheimer and associated symptoms.Int. J. Nutr. Pharmacol. Neurol. Dis.2012;2(2):84-91.
DOI: 10.4103/2231-0738.95927.
7. Ogbodo Onyebuchi Johna, Ihim Stella Amarachi, Agbo Precious Chinazomc, Echezona Adaezec, Mayur B. Kalee, Mohit D. Umaree, Aman B. Upaganlawar.Phytotherapy: A promising approach for the treatment of Alzheimer's disease.Pharmacological Research - Modern Chinese Medicine.2021; 2(2022):1-11.
DOI:10.1016/j.prmcm.2021.100030.
8. Parul Agarwal, Shashi Alok, Amreen Fatima and Prem Prakash Singh. Herbal Remedies for Neurodegenerative Disorder (Alzheimer's Disease): A Review.Int. J. Pharm. Sci. Res.2013;4(9):3328-3340.
DOI: 10.13040/IJPSR.0975-8232.4(9).3328-40.
9. P. Mecocci,C.Tinarelli, R.J. Schulz, M.C.Polidori. Nutraceuticals in cognitive impairment and Alzheimer's disease.Front. Pharmacol.2014;5(147):17-11.
DOI: 10.3389/phar.2014.00147.
10. Nusrat Zahan Bhuiyan, Md. Kamrul Hasan, ZimamMahmud,Md.Sabbir Hossain, Atiqur Rahman, Prevention of Alzheimer's disease through diet: An exploratory review.Science DirectMetabolism Open.2023;20:1-17.
DOI: 10.1016/j.metop.2023.100257.
11. Shunan Di, Miao Yu,HuiboGuan,Yanyan Zhou.Neuroprotective effect of Betalain against AlCl3-induced Alzheimer's disease in Sprague Dawley Rats via putative modulation of oxidative stress and nuclear factor kappa B (NF-κB) signaling pathway. Biomed Pharmacother.2021;137:1-8.
DOI: 10.1016/j.biopha.2021.111369

12. Jogender Mehla,PoojaGupta,Monika Pahuja, Deepti Diwanand, Diksha Diksha. Indian Medicinal Herbs and Formulations for Alzheimer's Disease, from Traditional Knowledge to Scientific Assessment. BrainSci.2020;10(964):1-31.
DOI:10.3390/brainsci10120964.
13. NafaaAlzobaidi,Huma Quasimi, Nasr A Emad, Abdulsalam Alhalmi,Maaz Naqvi. Bioactive Compounds and Traditional Herbal Medicine: Promising Approaches for the Treatment of Dementia. Degener Neurol Neuromuscul Dis.2021;11(2021):1-14.
14. Sushma Pradeepa, Anisha S. Jaina,Chandan Dharmashekaraa,Shashanka K. Prasada, Shiva Prasad Kollurb,AsadSyedc, Chandan Shivamallua. Alzheimer's Disease and Herbal Combination Therapy: A Comprehensive Review.JAD Reports.2020;4(2020):417–429.
DOI:10.3233/ADR-200228.
15. Rammohan V Rao, Olivier Descamps,Varghese John,Dale E Bredesen. Ayurvedic medicinal plants for Alzheimer's disease: a review. Alzheimer's Res.Ther.2012;4(22): 1-9.
DOI: http://alzres.com/content/4/3/22.
16. Yu-Yao Wu, Yan-Ming Xu, Andy T. Y. Lau.Epigenetic effects of herbal medicine.ClinicalEpigenetics.2023;15(85):1-21.
DOI: https://doi.org/10.1186/s13148-023-01481-1.
17. Toufik Abdul-Rahman, Wireko Andrew Awuah,TatianaMikhailova,Jacob Kalmanovich, Aashna Mehta. Antioxidant, anti-inflammatory and epigenetic potential of curcumin in Alzheimer's disease. BioFactors.2024;50:693–708.
DOI: 10.1002/biof.2039.
18. Yi-Ping Zhu,Ya Feng,TeLiu,Yun-Cheng Wu.Epigenetic Modification and Its Role in Alzheimer's Disease.Integr.Med.Int.2015;2:63–72.
DOI: 10.1159/000437329.
19. Chiara Villa and Romina Combi.Epigenetics in Alzheimer's Disease: A Critical Overview.Int.J.Mol.Sci.2024;25(5970):1-14.
DOI:https://doi.org/10.3390/ijms25115970.
20. Oliwia Stefaniak, Malgorzata Dobrzynska, Slawomira DrzymałaCzyzand, Juliusz Przyslawski.Diet in the Prevention of Alzheimer's Disease: Current Knowledge and Future Research Requirements.2022;14(4564):1-20.
DOI: https://doi.org/10.3390/nu14214564.

21. C.Castillo-Rangela, G. Marinc,D.L. Diaz-Chiguera,C.J. Zarate-Calderonb, I. Viveros-Martinezb, F.D.M.D.J. Caycho-Salazarb, J.G. Torres-Pasillasb, K.A. Hernández-Contrerasb, L.A. Vega-Quesadad, Y. Cano-Ortegad, L.Garcia-Hernandezb, L. Vasquez-Celaya.Animal models in Alzheimer's disease: Biological plausibility and mood disorders.Neurology Perspectives.2023:1-12.
DOI:https://doi.org/10.1016/j.neurop.2023.100110.
22. Dimitrios Athanasopoulos, George Karagiannisand Magda Tsolaki, Recent Findings in Alzheimer Disease and Nutrition Focusing on Epigenetics, American Society for Nutrition,2016;7:917–927.
23. Javad Sharifi-Rad,Simona Rapposelli,Simona Sestito, Jesus Herrera-Bravo, Alejandra Arancibia-Diaz, Luis A. Salazar, Balakyz Yeskaliyeva, Ahmet Beyatli,Gerardo Leyva-Gomez,Carlos Gonzalez-Contreras, Eda Sonmez Giirer, Miquel Martorell,Daniela Calina.Multi-Target Mechanisms of Phytochemicals in Alzheimer's Disease: Effects on Oxidative Stress, Neuroinflammation and Protein Aggregation.J. Pers.Med.2022; 12(1515):1-25.
DOI: https://doi.org/10.3390/jpm12091515.
24. Zhenying Yu, Hongyan Wu.Research Progress on the Therapeutic Mechanism of Tea Polyphenols in Neurodegenerative Diseases.JBM.2023;11:65-75.
DOI: 10.4236/jbm.2023.1111007.
25. Kokate C.K, Purohit A.P, Gokale S.B. Pharmacognosy. 43rd Edition, Pune (India): NiraliPrakashan, 2009, pp. A1-A6.
26. Khandelwal K.R. Practical Pharmacognosy Techniques and Experiments. Pune (India): Nirali Prakashan, 2000.

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